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Impact of Nonrandom Mating on Genetic Variance and Gene Flow in Populations With Mass Selection

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ABSTRACT

The mechanisms by which nonrandom mating affects selected populations are not completely understood and remain a subject of scientific debate in the development of tractable predictors of population characteristics. The main objective of this study was to provide a predictive model for the genetic variance and covariance among mates for traits subjected to directional selection in populations with nonrandom mating based on the pedigree. Stochastic simulations were used to check the validity of this model. Our predictions indicate that the positive covariance among mates that is expected to result with preferential mating of relatives can be severely overpredicted from neutral expectations. The covariance expected from neutral theory is offset by an opposing covariance between the genetic mean of an individual's family and the Mendelian sampling term of its mate. This mechanism was able to predict the reduction in covariance among mates that we observed in the simulated populations and, in consequence, the equilibrium genetic variance and expected long-term genetic contributions. Additionally, this study provided confirmatory evidence on the postulated relationships of long-term genetic contributions with both the rate of genetic gain and the rate of inbreeding (ΔF) with nonrandom mating. The coefficient of variation of the expected gene flow among individuals and ΔF was sensitive to nonrandom mating when heritability was low, but less so as heritability increased, and the theory developed in the study was sufficient to explain this phenomenon.

RECENT advances in quantitative genetic theory have allowed breeding schemes to consider the management of genetic variation objectively, simultaneously with the maximization of genetic gain. Such advances are highly relevant to breeding practice, not only for commercial schemes but also for those schemes that are orientated toward the conservation of genetic resources. These advances include the development of tractable, deterministic predictors of rates of inbreeding (ΔF), gene flow, and genetic gain (ΔG) for complex selected populations (WOOLLIAMS *et al.* 1999; WOOLLIAMS and BIJMA 2000), and operational tools for day-to-day selection decisions (WRAY and GODDARD 1994; MEUWISSEN 1997; GRUNDY *et al.* 1998).

However, the theory underpinning these tools has been developed primarily for random mating of the selected males and females and for a neutral locus where the genotypic frequencies in the offspring display no departure from Hardy-Weinberg (HW) proportions, other than that arising from the partitioning of the gene pool induced by two sexes (ROBERTSON 1965). However, the role of nonrandom mating, where some specific design is placed upon which male is mated to which

female, has been less well studied in this context. Although utilizing a mating design to minimize ΔF does not always lead to substantial deviations from HW proportions (SONESSON and MEUWISSEN 2000), much of the theory on genetic variation and the impact of nonrandom mating has been built up around the concept of departures from HW equilibrium (*e.g.*, CABALLERO and HILL 1992; SANTIAGO and CABALLERO 1995; WANG 1996) and the concepts of the avoidance of, or preference for, mating relatives.

The interpretation of the work on nonrandom mating, both its application and its impact, remains a subject of scientific debate. For example, in conservation, accepted practice uses minimum coancestry to minimize ΔF (CABALLERO *et al.* 1996; FRANKHAM *et al.* 2002), yet recent theoretical developments using genetic contributions show that the lowest ΔF with hierarchical matings is achievable when relatives are preferentially mated (SÁNCHEZ *et al.* 2003). In selected populations, there is clear evidence that mating designs are beneficial, although not all these designs define matings through pedigree, *e.g.*, factorial mating (WOOLLIAMS 1989). Several articles indicate that attention to the pedigree relationships within a mating design can be advantageous over random-mating schemes (*e.g.*, SANTIAGO and CABALLERO 1995; CABALLERO *et al.* 1996; SÁNCHEZ *et al.* 1999). However, the benefits of these methods have not always been quantified in predictable terms for their joint impact upon genetic gain and rates of inbreeding.

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Moreover, other studies on mating designs (TORO and PÉREZ-ENCISO 1990; KLIEVE *et al.* 1994; FERNÁNDEZ and TORO 1999) do not separate out the impact of specifying the matings from the impact of controlling only the overall contribution of each selected individual assuming random mating.

SANTIAGO and CABALLERO (1995) were successful in producing predictions of the effective population size [N_e , defined as $(2\Delta F)^{-1}$] in nonrandom mating populations undergoing mass selection, using an approach based upon the variance of allele frequencies. These authors considered nonrandom mating in the form of departures from HW equilibrium achieved through partial full-sib mating. However, WOOLLIAMS and BIJMA (2000) showed that, for random mating, an approach to predicting N_e using long-term genetic contributions was capable of extension to more complex selection schemes. To achieve such an extension with nonrandom mating requires an understanding of the expected gene flows of individuals based upon the inheritance of selective advantages, which in turn presupposes an understanding of the behavior of the genetic variation. There appears to be little published information on these topics.

Therefore, the main objective of this study is to advance the theoretical framework for predicting the impact of nonrandom mating for populations undergoing directional selection, providing a predictive model for the genetic variance and covariance among mates. The nonrandom mating is defined solely in terms of departures from HW proportions for neutral alleles, without reference to phenotypes. The impact is measured in terms of genetic parameters, such as genetic variance, expected gene flow, and ΔF , assuming the infinitesimal model and mass selection. In the course of this article, the opportunity to validate the developments of WOOLLIAMS and BIJMA (2000) for nonrandom mating is taken. The accuracies of the predictions of ΔF and ΔG and the validity of the framework are established with the help of stochastic simulations.

MATERIALS AND METHODS

Nonrandom mating and neutral theory: The correlation between uniting gametes due to the nonrandom mating of parents is an additional factor affecting heterozygosity over and above initial gene frequencies and their accumulated drift. Using the classical F -statistics of WRIGHT (1969), the expected fractional decrease in the heterozygosity for a given population (F_{IT}) can be related to two further statistics using the relationship $(1 - F_{IT}) = (1 - F_{IS})(1 - F_{ST})$, where F_{ST} is the fractional loss of heterozygosity due to the finiteness of the population census, and F_{IS} is the loss of heterozygosity due to the nonrandom mating of parents. The F_{IS} can be seen as a correlation of gene effects between homologous alleles in pairs of mating parents, *i.e.*, the correlation between alleles within infinitely many conceptual offspring derived from each of the pairs of mating parents (often denoted α_0 and hereafter in this study). Whereas, if conceived of as the correlation between alleles within successful offspring (*i.e.*, existing indi-

viduals), it measures the actual loss of heterozygosity due to the nonrandomness of the mating of the parents with nonzero contributions in the offspring generation (often denoted as α_I). Thus the former (α_0) is a potential correlation of uniting gametes from selected parents, whereas the latter (α_I) is a realized correlation and will be affected by the finite random sampling of gametes to form the offspring generation and by any artificial and/or natural selection of offspring before reaching the breeding population.

Under the assumption of completely neutral genes α_0 would tend to be equal to α_I . For neutral genes, when nonrandom mating results from a mix of full-sib mating and random mating, α_I (*i.e.*, $\alpha_I \approx \alpha_0 = \alpha$) can be related to the proportion of full-sib mating (denoted hereafter ϕ) by $\alpha = \phi / (4 - 3\phi)$ (GHAH 1969).

To obtain α_0 in a breeding population, let θ_{ij} be the coancestry (kinship) coefficient (LYNCH and WALSH 1998) of sire i and dam j , then following WRIGHT's (1969) equation $1 - \alpha_{0(ij)} = (1 - \theta_{ij}) / (1 - \bar{\theta})$, where $\bar{\theta} = F_{ST}$ is the average of all the entries in the matrix of coancestries among the parents (*i.e.*, i, j , and contemporaries), including self-coancestries and the reciprocals (COCKERHAM 1967). Thus $\alpha_{0(ij)}$ is defined for any pair of parents in relation to the complete set of selected parents. The term α_0 is the average $\alpha_{0(ij)}$ of the selected matings, irrespective of the fitness of the offspring, *i.e.*, as if all matings contribute an equal and large number of offspring to the next generation.

To obtain a summary value of α_I for a pedigreed population undergoing selection, we follow the same reasoning as above. Note that $\bar{\theta} = F_{ST}$ represents the average inbreeding coefficient if the offspring generation had been obtained by complete aggregation of the parental gene pool and sampling at random with replacement. Then for any individual offspring from that set of parents $\alpha_{I(k)} \approx F_{IS}$ and can be defined as $1 - \alpha_{I(k)} = (1 - F(k)) / (1 - \bar{\theta})$, where $F(k)$ is the coefficient of inbreeding of individual k , and is equal to $\theta_{\text{sire}(k), \text{dam}(k)}$. For the infinitesimal model, the Mendelian sampling deviation for an offspring k has a variance equal to

$$\begin{aligned} \frac{1}{2} \sigma_{A,0}^2 \left(1 - \frac{1}{2} F(\text{sire}(k)) - \frac{1}{2} F(\text{dam}(k)) \right) &= \frac{1}{2} \sigma_{A,0}^2 \left[\frac{1}{2} (1 - F(\text{sire}(k))) + \frac{1}{2} (1 - F(\text{dam}(k))) \right] \\ &= \frac{1}{2} \sigma_{A,0}^2 (1 - \bar{\theta}) \left(1 - \frac{1}{2} \alpha_{I(\text{sire}(k))} - \frac{1}{2} \alpha_{I(\text{dam}(k))} \right), \quad (1) \end{aligned}$$

where $\sigma_{A,0}^2$ is the initial variance of the breeding values. In the remainder of this study, the term $(1 - \bar{\theta})$ in Equation 1 is omitted for derivations and predictions, analogously to WOOLLIAMS *et al.* (1999) and WOOLLIAMS and BIJMA (2000). This omission allows the genetic variance to reach an equilibrium. Further details are given in the last section of MATERIALS AND METHODS.

The terms $\alpha_{I(k)}$ are used to define two related, but distinct, summary α_I : (i) $\alpha_{Ic} = \sum_k c_k \alpha_{I(k)}$, where c_k was the observed contribution of k to the selected offspring in the next generation, and (ii) $\alpha_{Ir} = \sum_k r_k \alpha_{I(k)}$, where r_k was the long-term genetic contribution (described in the following sections) of k . If we assume now that directional selection has taken place among families, then the direct equivalence between α_0 and α_I (irrespective of whether I_c or I_r) no longer holds for selective genes or neutral genes since selection success will depend on the α_I of the parents (CABALLERO *et al.* 1996).

Dynamics of genetic (co)variance for a selected trait under nonrandom mating: In this section, a model is developed to show that the impact of nonrandom mating on covariances between mates for selected traits and neutral traits may be qualitatively different and to describe the circumstances under which this can occur. In particular, it demonstrates that selection induces a negative covariance between true family means and Mendelian sampling terms, not only within individual

selected parents but also between a parent and its mate, thereby reducing genetic variance more than would be predicted by previously existing selection theory.

Consider a population with equal numbers of dams and sires, *i.e.*, a mating ratio of 1, mated in pairs to produce a deviation from HW equilibrium equal to α_0 on the basis of pedigree information alone. For the trait under selection, assume a heritability of h_0^2 when in HW equilibrium in an unselected base generation, with a phenotypic variance $\sigma_{P,0}^2 = 1$. It is assumed that the inheritance of the trait under selection can be described by an infinitesimal model and, for simplicity in the derivation of this model, that the nonrandom mating is achieved by managing ϕ , the proportion of full-sib matings. Note that this mating scheme does not produce half-sibs. From GHAI (1969), the neutral expectations are $\alpha_1 = \alpha_0 = \alpha$, and $\phi = 4\alpha/(1 + 3\alpha)$ for large populations.

Let P_i denote the phenotype of an individual i for the selected trait and B_i be the breeding value for a neutral trait, then the covariance between breeding values of mates is given by CABALLERO and HILL (1992) as $\text{cov}(B_{\text{sire}}, B_{\text{dam}}) = 2\alpha_0\sigma_B^2$, where σ_B^2 is the variance of the breeding values in the unselected and randomly mated base population. Now consider A_b , the breeding value for the selected trait. Then $A_i = \frac{1}{2}(A_{\text{sire}} + A_{\text{dam}}) + a_i = f_i + a_i$, where f_i is the true family mean, and a_i is the Mendelian sampling term. Define $\sigma_{A,t}^2$ as the variance of the breeding values at time t with $\sigma_{A,t}^2 = \sigma_{F,t}^2 + \sigma_M^2$, where $\sigma_{F,t}^2$ is the variance of the true family means at time t , and $\sigma_M^2 = \frac{1}{2}(1 - \alpha_1)h_0^2$ is the variance of the Mendelian sampling terms [note that the term $(1 - \theta)$ in Equation 1 is omitted here, and since $\sigma_{F,0}^2 = 1$, $h_0^2 = \sigma_{A,0}^2$]. For simplicity, the explicit dependence on t in the notation is neglected. For selection on phenotype P_b ,

$$\begin{aligned} f_i &= \frac{\sigma_F^2}{\sigma_P^2}P_i + \varepsilon_{i,1} \\ a_i &= \frac{\sigma_M^2}{\sigma_P^2}P_i + \varepsilon_{i,2}, \end{aligned} \quad (2)$$

where f_i and a_i are both partitioned into an expectation conditional on P_i and a residual (ε). Since $\text{cov}(f_b, a_b) = 0$, $\text{cov}(\varepsilon_1, \varepsilon_2) = -\sigma_F^2\sigma_M^2/\sigma_P^2$. Following the methods of BULMER (1980) for selection with the infinitesimal model, let superscript $*$ denote a parameter postselection on P_b , then $\text{cov}(f_i, a_i)^* = -\kappa\sigma_F^2\sigma_M^2/\sigma_P^2$ since $\sigma_F^{2*} = (1 - \kappa)\sigma_F^2$, where κ is the variance reduction coefficient. This has a direct analogy to linkage disequilibrium, where selection on P_i induces negative covariance between the effects of different loci, and where the induction of this covariance is not dependent on mating procedures. The regression of a_i on f_i after selection is

$$b_{af} \approx -\kappa\sigma_F^2\sigma_M^2/(\sigma_P^2\sigma_F^{2*}), \quad (3)$$

where $\sigma_F^{2*} = \sigma_F^2(1 - \kappa\sigma_F^2/\sigma_P^2)$ is the variance of true full-sib family means after selection. Note $b_{af} < 0$, and $b_{af} \neq 0$ after selection.

When allocating mates (i, j) using the pedigree alone,

$$\begin{aligned} \text{cov}(A_b, A_j) &= \text{cov}(f_i + a_i, f_j + a_j) \\ &= \text{cov}(f_i, f_j) + \text{cov}(f_i, a_j) + \text{cov}(a_i, f_j) + \text{cov}(a_i, a_j). \end{aligned}$$

Substituting $a_j = b_{af}f_j + \varepsilon_j$ and analogously for a_i , and using ϕ to estimate the covariance between mates,

$$\begin{aligned} \text{cov}(A_i, A_j) &= \phi\sigma_F^{2*} + 2b_{af}\phi\sigma_F^{2*} + b_{af}^2\phi\sigma_F^{2*} \\ &= \phi\sigma_F^{2*}(1 + b_{af})^2. \end{aligned} \quad (4)$$

In the absence of selection, this is simply $\phi\sigma_F^2$. Therefore, with selection, since (i) $\sigma_F^{2*} < \sigma_F^2$ and (ii) $b_{af} < 0$, the covariance achieved between the breeding values of mates for the trait of selection is less than that for neutral traits. The implication

from Equation 3 is that the covariance between mates for the selected trait may be dramatically reduced below what is expected when b_{af} becomes more strongly negative, when (i) selection intensity is large, since $\kappa \rightarrow 1$, and when (ii) h_0^2 is large, since σ_M^2/σ_P^2 is large. The term $(1 + b_{af})^2$ is relatively insensitive to α for mass selection, but is sensitive to h_0^2 . For $\kappa = 0.64$, $\alpha = 0.06$, $(1 + b_{af})^2$ takes values of 0.87, 0.73, 0.57, 0.38, and 0.18 for $h_0^2 = 0.2, 0.4, 0.6, 0.8$, and 0.99, respectively (from Equation 3 and genetic variances obtained from simulated populations); for $\alpha = 0.24$, the values are 0.90, 0.77, 0.62, 0.42, and 0.18.

Since $\sigma_M^{2*} = \sigma_M^2(1 - \kappa\sigma_M^2/\sigma_P^2)$, $\sigma_F^{2*} = \sigma_F^{2*} + 2\text{cov}(f_b, a_b)^* + \sigma_M^{2*} = \sigma_A^2(1 - \kappa h^2)$, and for their offspring $A_{\text{off}} = \frac{1}{2}(A_i + A_j) + a_{\text{off}}$:

$$\sigma_A^2 = \frac{1}{2}(\sigma_A^{2*} + \phi(1 + b_{af})^2\sigma_F^{2*}) + \sigma_M^2. \quad (5)$$

This will move to equilibrium over generations so that the effect of selection is counterbalanced by the addition of σ_M^2 (analogously to BULMER 1980, p. 155).

Consequently, for the selected trait, the total observed additive variance may decline even as α_0 increases (demonstrated in the RESULTS), although α_0 is superficially increasing one component of the variation. This is a phenomenon associated with linkage disequilibrium and arises from (i) a lower Mendelian sampling variance replenishing the genetic variation lost due to selection in each generation and (ii) the induction of negative covariance between the Mendelian sampling term of a parent and the true family mean of its mate.

Predictions of rate of inbreeding and genetic gain through the concept of long-term genetic contributions: The genetic contribution of an ancestor k (denoted r_k) to a descendant j is the proportion of genes carried by j that are expected to derive by descent from the ancestor k . A descendant's breeding value can be decomposed into a sum of Mendelian sampling deviations from all ancestors, with the weighting for ancestor k 's Mendelian deviation being r_k . For a mixing population, after a sufficiently large number of generations, k 's genetic contribution to all individuals within the population approaches the same stable and constant value across generations. In the remainder of the text, the stable genetic contributions from distant ancestors are referred to as "long-term genetic contributions." The long-term genetic contributions will reflect differences among individual ancestors arising from their respective selective advantages together with cumulative chance factors across generations. Therefore, long-term genetic contributions model the gene flow of individual ancestors through the population.

The asymptotic ΔF for nonrandom mating can be derived through its theoretical relationship with the sum of squared long-term genetic contributions,

$$\Delta F = \frac{1}{4}(1 - \alpha_1)\sum_k r_k^2 \quad (6)$$

(WOOLLIAMS and BIJMA 2000). The rate of genetic gain (ΔG) per generation is also related to long-term genetic contributions since sustained genetic gain arises through the generation of covariance between long-term genetic contributions and Mendelian sampling deviations,

$$\Delta G = \sum_k r_k a_k \quad (7)$$

(WOOLLIAMS *et al.* 1999), where the sum is taken over a generation of ancestors. Therefore, the concept of long-term genetic contribution bridges the loss of heterozygosity and the generation of genetic gain for any deviation from random mating given by α_1 .

For mass selection, the selective advantages for an ancestor are its own breeding value and those of its mates. This set of

selective advantages influences not only the breeding success of the resulting offspring from that given ancestor, but also that of subsequent descendants. This dependence of the gene flow on the selective advantage can be expressed as a conditional expectation (μ_k), *i.e.*, as a function of the selective advantages. For truncation selection based upon phenotype, μ_k can be satisfactorily modeled as a linear relationship between the genetic contribution and the breeding values,

$$\mu_k = \gamma + \beta_{(r,A)}(A_k - \bar{A}) + \beta'_{(r,A)} \sum_{\text{mates}} (A_{\text{mate}(k)} - \bar{A}') \quad (8)$$

(WOOLLIAMS *et al.* 1999), where the terms \bar{A} and \bar{A}' are the mean breeding values of the selected individuals for the sex of k and its mates' sex, respectively. For discrete generations, $\gamma = (2N_s)^{-1}$ and $(2N_d)^{-1}$ for N_s sires and N_d dams, respectively, and is independent of h_0^2 and α_i . When $N_s = N_d = N$ with no mating hierarchy, $\beta_{(r,A)} = \beta'_{(r,A)}$, and from here onward, we denote this as β . Therefore under these two conditions, discrete generations and N mating pairs, the only parameters varying with the breeding scheme are the slope of the relationship β and the genetic variance among selected individuals derived from σ_A^2 (WOOLLIAMS *et al.* 1999). Equation 8 becomes

$$\mu_k = \gamma + \beta[(A_k - \bar{A}) + (A_{\text{mate}(k)} - \bar{A}')]. \quad (9)$$

Thus β is the regression coefficient of the long-term contribution of an individual on the sum of its breeding value and that of its mate. The impact of the selective advantage on the gene flow (and, ultimately, on ΔF) can then be measured by the coefficient of variation (CV) of the conditional expectation:

$$CV(\mu_k) = 2N\beta\sqrt{2(\sigma_A^{2*} + \phi(1 + b_{af})^2\sigma_F^{2*})}. \quad (10)$$

Population model and procedures for stochastic simulation:

This section describes the general population model and selection procedures for which predictions and simulations will be compared. The population was reproduced in discrete generations with a constant breeding size of N_s sires and N_d dams and a mating ratio of dams to sires of 1 in all generations ($N_s = N_d = N$). Each dam mothered n_0 offspring, all full-sibs, and comprising equal numbers of male and female candidates. Selection was upon phenotype P , which was the sum of breeding value A and an environmental deviation.

For simulation, a noninbred and unrelated base population was generated with $\sigma_{P,0}^2 = 1$. Each founder's A was taken from $N(0, \sigma_{A,0}^2)$, where $\sigma_{A,0}^2$ is the initial genetic variance (since $\sigma_{P,0}^2 = 1$, initial heritability $h_0^2 = \sigma_{A,0}^2$). In subsequent generations, each new breeding value was the sum of $\frac{1}{2}(A_{\text{sire}} + A_{\text{dam}})$ and a Mendelian sampling deviation. The latter term was drawn from $N(0, \frac{1}{2}\sigma_{A,0}^2(1 - \frac{1}{2}\alpha_{I(\text{sire})} - \frac{1}{2}\alpha_{I(\text{dam})}))$, where $\alpha_{I(\text{sire})}$ and $\alpha_{I(\text{dam})}$ are due to the nonrandom mating between grandparents. An environmental deviation sampled from $N(0, 1 - \sigma_{A,0}^2)$ was added to each individual's breeding value to obtain P . The simulations omitted the term $(1 - \bar{\theta})$ in Equation 1, as previously indicated in the first section. Consequently, the genetic variance, and hence the variance in the selective advantages, in the simulated populations reached an equilibrium upon which to base stable predictions.

Selected individuals were mated following a mating design with nonrandom mating based upon α_0 (as defined earlier), which was carried out systematically in all generations except in the base population, where founders were randomly allocated in pairs. The allocation of mates was decided in such a way that α_0 was as close as possible to a target value α_{Ofix} . This process involved a search throughout the feasible set of matings, carried out by the *simulated annealing* technique (PRESS *et al.* 1992), to minimize the objective function given by $(\alpha_0 - \alpha_{\text{Ofix}})^2$. A random sample of matings was used as a starting point. The maximum feasible value for α_0 is 1, which can be attained by multiple generations of close inbreeding

leading to sublining. For the benefit of a more general scheme, the upper limit of α_{Ofix} was <1 in this study. On the other extreme, the lowest possible value of α_0 in finite populations lies much closer to what is expected for random-mating populations, due to the fact that the avoidance of inbreeding is constrained in the long term by the genetic depletion caused by drift, as pointed out by CABALLERO and HILL (1992). The values of α_{Ofix} used in the simulation were $-0.03, 0, 0.03, 0.06, 0.12, 0.18$, and 0.24 .

Long-term genetic contributions were calculated for an ancestral generation born after 20 generations of selection from the unselected base and upon the cohort of descendants born 20 generations after that ancestral generation. This guaranteed attainment of equilibrium of genetic variances in all the cases with $\alpha_{\text{Ofix}} \leq 0.12$. With more extreme α_{Ofix} , however, a longer period of time was needed before such equilibrium is reached (SANTIAGO and CABALLERO 1995). For these cases, 20 further generations were bred before establishing the ancestral generation, although it was found unnecessary to extend the period of time for obtaining summary statistics for the converged contributions (*i.e.*, 20 generations from ancestors to descendants). Observed long-term genetic contributions were used to calculate the predictions of ΔF and ΔG from Equations 6 and 7.

The values of achieved α_0 , α_{Ic} , α_{Ir} , and σ_A^2 and the genetic covariance among mates were recorded for each generation of the simulated populations, together with the observed ΔF , ΔG , Σr_k^2 , and $\Sigma r_k a_k$ (Equation 7). The observed ΔF and ΔG were obtained as the average rate of the last 20 generations of the simulated populations. β was obtained by multiple regression of the long-term contribution of ancestors on their own breeding value and that of their mates; as no significant difference in the regression coefficients was found, as predicted, the value used in the text is the average of the two values. The proportion of full-sib matings (ϕ) was also recorded in each simulated population. Results were averaged over 1000 replicates and standard errors derived from the variance between replicates. The values of basic parameters used in the simulations were $h_0^2 = \{0.01, 0.05, 0.1, 0.2, 0.4, 0.6, 0.8, \text{ and } 0.99\}$, $N = \{32, 64, \text{ and } 128\}$, and $n_0 = \{4, 8, \text{ and } 16\}$.

RESULTS

Expected *vs.* observed degree of nonrandom mating:

The degree of nonrandom mating is described in this section, in terms of (i) the two distinct summary α_i 's (*i.e.*, α_{Ic} and α_{Ir}) *vs.* α_{Ofix} and (ii) the expected and observed proportion of full-sib matings (ϕ_{exp} and ϕ_{obs} , respectively).

For item i, Table 1 shows that substantial deviations between α_{Ir} and α_{Ic} occurred, with $\alpha_{Ir} < \alpha_{Ic}$ as h_0^2 increased and α_{Ofix} increased. Statistically significant but slight differences with $\alpha_{Ir} > \alpha_{Ic}$ also occurred with $h_0^2 = 0.01$. Where $\alpha_{Ir} < \alpha_{Ic}$, the substantial difference indicates a negative covariance between the individual's long-term genetic contribution and α_i . Thus, those individuals with low values of α_i , consequently with a relatively greater Mendelian sampling variance in their offspring, had a selective advantage over their contemporaries and, therefore, a greater long-term genetic contribution. This association between long-term genetic contributions and the variation in α_i within a scheme became more evident as selection became more intense, through both large n_0 and/or large mating ratios (*i.e.*, $N_s <$

TABLE 1

Target departures from HW proportions (α_{Ofix}) vs. observed departures measured as the asymptotic average of α_i weighted by the observed contribution as parent to the selected offspring in the next generation (α_{Ic}) and the asymptotic average of α_i weighted by the long-term genetic contribution (α_{Ir}), with phenotypic selection and $N = 32$, for different α_{Ofix} , family size (n_0), and initial heritabilities (h_0^2)

n_0	α_{Ofix}	$h_0^2 = 0.01$		$h_0^2 = 0.2$		$h_0^2 = 0.4$	
		α_{Ic}	α_{Ir}	α_{Ic}	α_{Ir}	α_{Ic}	α_{Ir}
4	-0.03	-0.0266	-0.0266	-0.0273	-0.0273	-0.0278	-0.0278
	0	0.0000	0.0000	0.0016	0.0015	0.0019	0.0021
	0.06	0.0609	0.0620	0.0686	0.0711	0.0689	0.0679
	0.12	0.1225	0.1271	0.1340	0.1344	0.1327	0.1220
	0.24	0.2455	0.2572	0.2597	0.2306	0.2550	0.2095
16	-0.03	-0.0289	-0.0289	-0.0296	-0.0294	-0.0295	-0.0295
	0	0.0006	0.0006	0.0065	0.0071	0.0075	0.0069
	0.06	0.0635	0.0671	0.0787	0.0739	0.0744	0.0594
	0.12	0.1274	0.1338	0.1414	0.1144	0.1311	0.1022
	0.24	0.2489	0.2557	0.2538	0.1767	0.2376	0.1422

Standard errors are $<0.25\%$ ($n_0 = 16$) and 0.29% ($n_0 = 4$).

N_D , results not shown), since high selection intensity promotes the proliferation of favored lineages.

For item ii, Figure 1 shows that high values of α_{Ofix} led to important deviations between observed and expected values of ϕ , with $\phi_{\text{obs}} < \phi_{\text{exp}}$, although a good fit was obtained for intermediate α_{Ofix} . Note that the simulations were implemented through general algorithms for nonrandom mating so that α_0 was attained through multiple sources of nonrandomness rather than through full-sib mating alone, although since $N_s = N_D$ there were no half-sibs. For the lower extreme shown in Figure 1, with $\alpha_{\text{Ofix}} = 0$, ϕ_{obs} was >0 although $\phi_{\text{exp}} = 0$. This should be expected for two reasons: in a small population the probability of a full-sib mating is not

vanishingly small as is explicitly assumed in the result of GHAI (1969), and random allocation of mates with two sexes will result in a marginally negative α_0 (ROBERTSON 1965), requiring some full-sib matings in compensation.

Effects of nonrandom mating on the genetic (co)variances for the selected trait: In this section, we describe the effects of nonrandom mating on the *selected trait* for (i) the genetic covariance among mates and (ii) the genetic variance. Simulated genetic covariance among mates is shown in Figure 2 for a range of α_{Ofix} and h_0^2 , along with the respective neutral expectation under random selection (*i.e.*, $h_0^2 = 0$). The values shown in Figure 2 are $\frac{1}{2}\text{cov}(A_i, A_j)/\sigma_{A,0}^2$, since they have an expectation

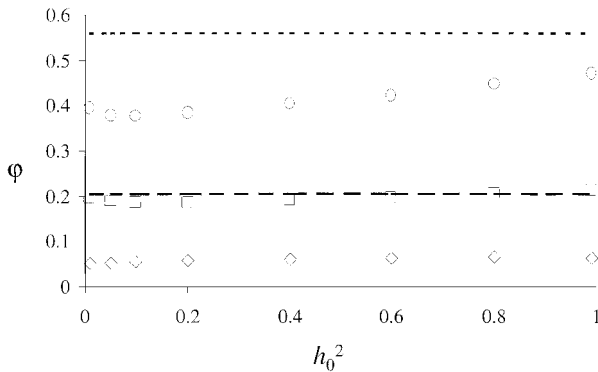


FIGURE 1.—Relationship between the proportion of full-sib matings (ϕ) and the initial heritability (h_0^2), for phenotypic selection with different values of α_{Ofix} . The lines are predicted relationships using $\phi = 4\alpha_{\text{Ofix}}/(1 + 3\alpha_{\text{Ofix}})$, and the points are observations from simulated populations ($N = 32$, $n_0 = 16$). Predictions are: zero with $\alpha_{\text{Ofix}} = 0$; ---, $\alpha_{\text{Ofix}} = 0.24$; —, $\alpha_{\text{Ofix}} = 0.06$. Simulations are: \circ , $\alpha_{\text{Ofix}} = 0.24$; \square , $\alpha_{\text{Ofix}} = 0.06$; \diamond , $\alpha_{\text{Ofix}} = 0$.

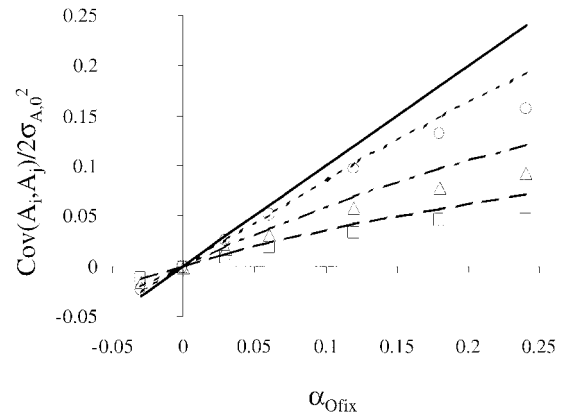


FIGURE 2.—Relationship between the covariance between the breeding values of mates ($\text{cov}(A_i, A_j)$), scaled by $2\sigma_{A,0}^2$, and α_{Ofix} , for phenotypic selection with different initial heritabilities (h_0^2). The lines are predicted relationships using Equation 4, and the points are observations from simulated populations ($N = 32$, $n_0 = 4$). Predictions are: —, $h_0^2 = 0$ (neutral theory); ---, $h_0^2 = 0.05$; ···, $h_0^2 = 0.2$; — ·, $h_0^2 = 0.4$. Simulations are: \circ , $h_0^2 = 0.05$; Δ , $h_0^2 = 0.2$; \square , $h_0^2 = 0.4$.

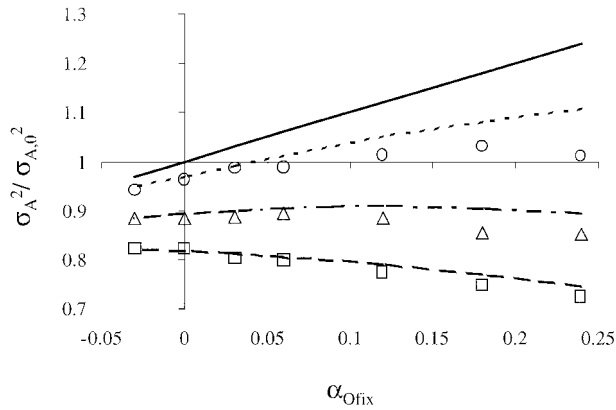


FIGURE 3.—Relationship between equilibrium genetic variance prior to selection within a generation (σ_A^2), scaled by $\sigma_{A,0}^2$, and α_{Ofix} , for phenotypic selection with different initial heritabilities (h_0^2). The lines are predicted relationships using Equation 5, and the points are observations from simulated populations ($N = 32$, $n_O = 4$). Predictions are: —, $h_0^2 = 0$ (neutral theory); ---, $h_0^2 = 0.05$; - · -, $h_0^2 = 0.2$; · · · ·, $h_0^2 = 0.4$. Simulations are: ○, $h_0^2 = 0.05$; △, $h_0^2 = 0.2$; □, $h_0^2 = 0.4$.

of α_{Ofix} for neutral theory. The clear result is that directional selection reduces the covariance of mates from what is expected under neutral theory. Furthermore, this reduction is well predicted using Equation 4 and $\phi = 4\alpha/(1 + 3\alpha)$ (with α replaced by α_{Ofix}). In the examples shown in Figure 2, the covariance among mates remains approximately linearly related to α_{Ofix} , but the slope of this relationship becomes lower as the heritability increased from 0 to 0.4. The application of Equation 4 with $b_{df} = 0$ also results in a lower covariance than that expected from neutral theory, but results in overestimates of the covariance; e.g., for $h_0^2 = 0.40$ and $\alpha_{Ofix} = 0.18$, the observed scaled value was 0.050, and Equation 4 predicts 0.082 and 0.057 with and without setting $b_{df} = 0$, respectively.

Given that the genetic covariance among mates contributes to the genetic variance under nonrandom mating, a reduction in the former component from that predicted by neutral theory will potentially result in a reduction in the latter. This is confirmed in Figure 3 with stochastic simulations and predictions using Equation 5. With selection, the genetic variance in the population can be lower with $\alpha_{Ofix} > 0$ than when comparable selection is practiced in randomly mated populations. The predictions from Equation 5 tend to overpredict the genetic variance by more than is expected from reductions due to finite sample size alone.

Effects of nonrandom mating on the expected gene flow: Figure 4 shows the relationship between the regression coefficient of long-term genetic contributions on the sum of selective advantages of mating pairs and α_{Ofix} . For a given α_{Ofix} , for all combinations of h_0^2 and n_O studied, β increased as n_O increased (and hence selection intensity) and decreased as h_0^2 increased. The relation-

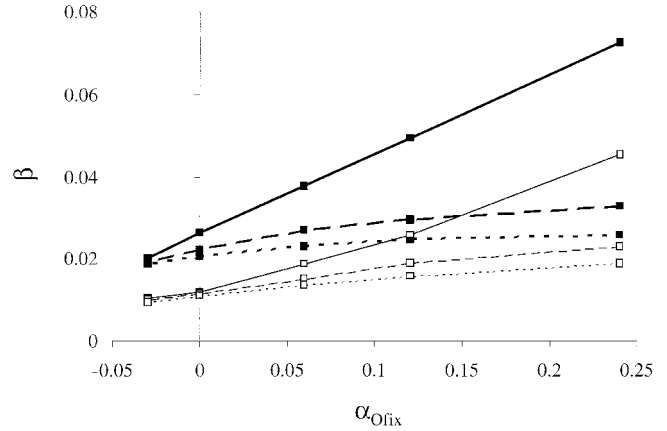


FIGURE 4.—Relationship between β and α_{Ofix} , for phenotypic selection with different initial heritabilities (h_0^2) and family sizes (n_O). The lines are observations from simulated populations ($N = 32$), where ■ with thick lines are $n_O = 16$; □ with thin lines, $n_O = 4$; —, $h_0^2 = 0.01$; - · -, $h_0^2 = 0.2$; · · · ·, $h_0^2 = 0.4$.

ships of β with h_0^2 and n_O are fully consistent with the findings of WOOLLIAMS *et al.* (1999) for random mating.

It may be expected from neutral theory that increasing α_O would increase the regression on the selective advantage since selected offspring will be more likely to be mated to relatives, so reinforcing the strength or weakness of the inherited selective advantage, *i.e.*, the mean parental breeding value, not only predicts the breeding value of its offspring but also predicts that of its offspring's mate. This is clearly the case for low h_0^2 ; for example, for $h_0^2 = 0.01$ and $n_O = 16$, as α_{Ofix} increased from 0 to 0.24, β increased more than threefold in a linear relationship with α_{Ofix} . However as h_0^2 increased, the slope of this relationship with α_{Ofix} was substantially lower. For $n_O = 16$ and $h_0^2 = 0.99$, no increase in β with α_{Ofix} was observed (result not shown). This reduction in the slope of the relationship between β and α_{Ofix} is directly related to the phenomenon displayed in Figure 2 concerning the covariance between mates as described above: when α_{Ofix} and h_0^2 are large, the covariance is lower than that expected from neutral theory and the selective advantage is poorer than expected at predicting the selective advantage of the offspring's mate.

The impact of the nonrandom mating on the expected gene flows conditional on the selective advantage (*i.e.*, the sum of the breeding values of an individual and its mate) is shown in Figure 5, measured by the CV of μ_k (see Equation 10). The values presented in Figure 5 use parameters in Equation 10 estimated from the simulations. For $\alpha_{Ofix} = 0$, it is clear that the impact of the selective advantage on gene flow is greatest when $0.4 < h_0^2 < 0.6$, with close to 4-fold impact compared to $h_0^2 = 0.01$. The impact of the selective advantage is increased when α_{Ofix} increases, but is more sensitive to changes in α_{Ofix} when h_0^2 is low. Therefore, when $\alpha_{Ofix} = 0.24$, the maximum impact is close to $h_0^2 = 0.2$ and is only 1.5-fold greater compared to $h_0^2 = 0.01$.

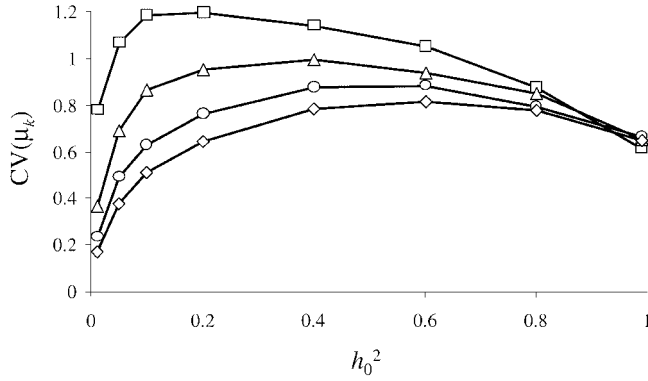


FIGURE 5.—Relationship between CV of expected long-term genetic contributions [$CV(\mu_k)$] and initial heritability (h_0^2), for phenotypic selection with different values of α_{Ofix} . The lines are modeled using Equation 10 with parameters estimated from the simulations ($N = 32$, $n_o = 16$). The different lines are: \square , $\alpha_{Ofix} = 0.24$; Δ , $\alpha_{Ofix} = 0.06$; \circ , $\alpha_{Ofix} = 0$; \diamond , $\alpha_{Ofix} = -0.03$.

Effect of nonrandom mating on predictions of ΔF and ΔG based on long-term genetic contributions: The effect of nonrandom mating on ΔF is shown in Figure 6 and Table 2 contrasts predictions using Equation 6 for two different selection intensities. The pattern of relationship between ΔF and h_0^2 and α_{Ofix} is very similar to Figure 5, in that the h_0^2 with the maximum ΔF becomes lower as α_{Ofix} increases, and ΔF increases very rapidly for small h_0^2 when α_{Ofix} is large.

Predictions of ΔF using Equation 6 always underestimated the observed ΔF , but this is expected by a fraction approximately equal to $2\Delta F$ (WOOLLIAMS and BIJMA 2000). When this is accounted for (as in Table 2), the serious errors occur only when selection intensity and α_{Ofix} are high. The pattern of these errors is similar to the cases in Table 1, where α_{lc} and α_{lr} show serious discrepancies. The predictions shown use α_{lr} in Equation 6, and not α_{lc} , since α_{lr} provided more reliable predictions than α_{lc} . Where serious discrepancies occurred between the observed ΔF and ΔF predicted from Equation 6, the prediction error could be approximately halved (results not shown) by modifying Equation 6 to be $\Delta F = \frac{1}{4} \sum_k r_k^2 (1 - \alpha_{l(k)})$, so that each individual's squared contribution was scaled by the individual's own α_l . This partially overcame the covariance that was described above between r_k and $\alpha_{l(k)}$. Finally, predictions of ΔG (not shown) obtained from Equation 7 were accurate for most of the assessed cases, and often their errors were $<5\%$ within the range of parametric settings investigated.

DISCUSSION

This article has provided a novel model for predicting the impact of nonrandom mating on the covariance among mates of populations undergoing selection. Examination of the predictions obtained from this model

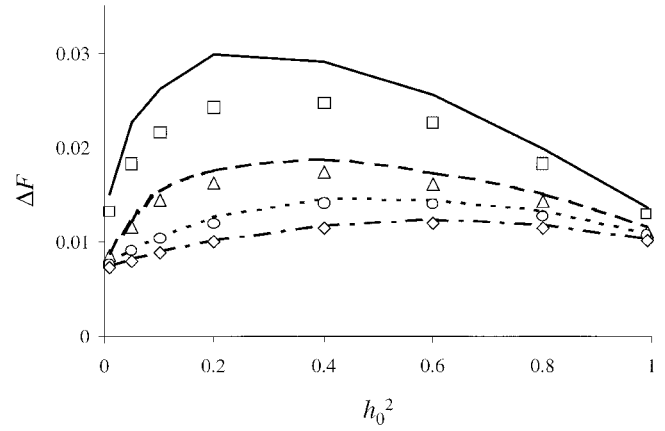


FIGURE 6.—Relationship between asymptotic rate of inbreeding (ΔF) and initial heritability (h_0^2), for phenotypic selection with different values of α_{Ofix} . The lines are predicted relationships using Equation 6, and the points are observations from simulated populations ($N = 32$, $n_o = 16$). Predictions are: —, $\alpha_{Ofix} = 0.24$; --, $\alpha_{Ofix} = 0.06$; ---, $\alpha_{Ofix} = 0$; -.-, $\alpha_{Ofix} = -0.03$. Simulations are: \square , $\alpha_{Ofix} = 0.24$; Δ , $\alpha_{Ofix} = 0.06$; \circ , $\alpha_{Ofix} = 0$; \diamond , $\alpha_{Ofix} = -0.03$.

showed that extrapolating expectations of genetic variance and covariance among mates for a neutral trait with nonrandom mating can be qualitatively wrong, with deviations toward severe overprediction. Deviations were largest when heritability and selection intensity were large and there was a strong preferential mating of relatives. While nonrandom mating had a considerable effect upon the impact of selective advantage for low heritability, as measured by the regression of genetic contributions on the selective advantage and the CV of the expected gene flow conditional on the selective advantage, the phenomenon described by the model substantially reduces this effect for moderate heritabilities. Furthermore, the study showed that high selection intensity can induce a negative covariance between the long-term genetic contribution of an ancestor and its α_l , particularly when α_o is large, and suggested that selection acts to attenuate the strong preferential mating of relatives.

A logical starting point for interpreting the results of deviations from neutral expectations is the genetic covariance achieved among mates for a selected trait when nonrandom mating was practiced. Naively, the preferential mating of relatives would be expected to result in a clear positive genetic covariance among breeding values, since for a neutral trait this covariance has an expectation equal to $2\alpha_o\sigma_{A,0}^2$ (e.g., CABALLERO and HILL 1992), and this is also shown in our simulations for neutral traits, so provides a methodological validation for our study. However, the predictive model for the covariance among mates showed that inducing such a covariance by using pedigree information during selection will lead to a covariance of opposite sign between the genetic mean of an individual's family and the Men-

TABLE 2
Simulated *vs.* predicted rates of inbreeding

n_O	α_{Ofix}	$h_0^2 = 0.01$		$h_0^2 = 0.2$		$h_0^2 = 0.4$	
		Sim($\times 100$)	%Prd	Sim($\times 100$)	%Prd	Sim($\times 100$)	%Prd
4	-0.03	0.59	0.8	0.65	0.9	0.69	1.3
	0	0.60	1.2	0.69	1.6	0.74	1.0
	0.06	0.62	0.8	0.83	1.9	0.87	2.7
	0.12	0.67	0.9	1.00	2.5	1.02	4.7
	0.24	0.82	2.9	1.37	10.8*	1.33	9.2*
16	-0.03	0.74	1.5	1.02	2.2	1.17	2.9
	0	0.77	1.8	1.26	6.2	1.45	3.6
	0.06	0.89	3.7	1.76	7.3	1.87	7.4
	0.12	1.07	5.9*	2.18	10.1*	2.18	11.1*
	0.24	1.50	12.9*	2.98	18.7*	2.91	15.3*

Simulated (Sim) rate of inbreeding ($\times 100$), together with prediction errors from using Equation 6, for phenotypic selection and $N = 32$, different target departures from Hardy-Weinberg proportions (α_{Ofix}), family sizes (n_O), and heritabilities (h_0^2) is shown. * indicates when the difference was $> (5\Delta F) \times 100$. Standard errors of Sim($\times 100$) were < 0.01 , except for $\alpha_{\text{Ofix}} = 0.24$ where the standard errors were < 0.03 . Prediction errors are expressed as a percentage of deviation (%Prd) = $100 \times ([\text{Sim} - \text{Prd}]/\text{Sim})$, where Prd comes from Equation 6.

delian sampling term of its mate. Therefore when there is a preferential mating, or avoidance, of relatives the induced covariance is offset by this opposing covariance, which can be substantial. This is in addition to another opposing effect that is directly analogous to BULMER (1980) by which the change in the Mendelian sampling variance with α_1 has an impact on the replenishment of the genetic variation that is lost through selection in each generation.

The mechanism underlying this model was potentiated as the intensity of selection increased and as the heritability increased. In this article where the results presented have been concerned with selection upon phenotype, the heritability represented the squared accuracy of selection and, together with the value of α_1 , determined the split in information between the pedigree and the Mendelian sampling term (important in Equations 2, 3, and 5). In more general selection schemes the power of the mechanism would depend on the balance of pedigree information on a candidate and information on its Mendelian components and the use made of such information (*e.g.*, within-family selection should not generate such a mechanism), rather than on the accuracy alone.

While the model provides an explanation of some of the results, it has some limitations. First, while its predictions are more credible than those based on neutral theory, the precision leaves some scope for believing that other mechanisms may be operating. Of greater significance is that the covariance between mates is estimated by assuming that the proportion of full-sib mating was that predicted by GHAI's (1969) formula. The use of this formula has two problems: (i) it is limited to schemes with equal numbers of males and females since

it cannot cope with nonrandomness coming from other sources such as preference/avoidance of half-sibs and (ii) the predictions provided by Ghai while broadly reliable were not without error. In the model, Ghai's formula was used to translate the desired α_0 to an expected covariance among the true family means of mates in the selected population; consequently, some improvement might arise from a more general approach to this relationship.

The reduction in covariance between mates arising with selection has direct consequences for the additive genetic variance and for the relationship between long-term genetic contributions and the selective advantage. Both are reduced below expectations based upon neutral theory. The impact on genetic variance is sufficient for the equilibrium genetic variance (*i.e.*, where Mendelian sampling variance is not reduced each generation as inbreeding progresses) to be less for preferential mating of relatives than for random mating when h_0^2 is high, a qualitative difference. The regression of the long-term genetic contribution on the sum of the ancestral breeding value and the average of its mates would also be expected to increase under neutral theory, since this has a covariance not only with the offspring's breeding value but also with that of the offspring's mate. Note that this expectation arises from the nonrandom mating in the offspring generation, not the ancestors: in the ancestor's generation the nonrandom mating is fully accounted for by regression on both parents. However, if the covariance between mates is reduced then so is the predictive value of the ancestor's selective advantages.

The impact of h_0^2 on the CV of the expected gene flow is similar to the impact of h_0^2 on ΔF that was observed in this study and that of SANTIAGO and CABAL-

lero (1995). This relationship shows a much greater sensitivity to nonrandom mating when the heritability is low than when it is either moderate or high. This can be explained by the behavior of the covariance between mates and its separate consequences for β and σ_A^2 as described, since changes in both parameters are responsive to changes with α_1 when the heritability is low, but decrease in sensitivity as heritability increases. The similarity between $CV(\mu_k)$ and ΔF in their relationship with α_1 may be anticipated since in Equation 6, which relates ΔF to squared contributions, the term $E[\Sigma r_k^2]$ is equivalent to $E[\Sigma(\mu_k^2 + \sigma_k^2)]$, where μ_k and σ_k^2 are the mean and variance of the contributions conditional upon the selective advantages. WOOLLIAMS and BIJMA (2000) showed that $\sigma_k^2 \approx \mu_k^2$ for random mating, but an analogous relationship has not been established for nonrandom mating, although it has been established that σ_k^2 will depend upon α_1 : avoidance of relatives reduces σ_k^2 (e.g., WANG 1997), whereas preferential mating of relatives increases σ_k^2 (e.g., CABALLERO and HILL 1992).

In conclusion, this study has described mechanisms that influence the covariance observed between mates for a trait that is subject to selection when mating is nonrandom. In particular, the covariance is substantially less than that expected from neutral theory, particularly when the heritability is moderate or high, and this has consequences for the observed additive genetic variance, the scale of expected gene flow that is directly attributable to the selective advantage, and ΔF . The observed sensitivity to nonrandom mating of the latter two phenomena when heritability is low can be explained with reference to neutral theory, and the study shows that it is the lack of sensitivity for moderate to high heritabilities that required the development of theory.

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